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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/067,121	11/13/2001	Kevin R. McIntosh	640100-441	5983

7590

09/09/2004

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EXAMINER

BELYAVSKIY, MICHAIL A

ART UNIT

PAPER NUMBER

1644

DATE MAILED: 09/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/067,121	Applicant(s) MCINTOSH ET AL.	
	Examiner Michail A Belyavskyi	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 August 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 71,72 and 96-117 is/are pending in the application.
- 4a) Of the above claim(s) 72,116 and 117 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 71 and 96-115 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 08/02/2004 is acknowledged.

Claims 71, 72, 96-117 are pending.

Claims 72, 116 and 117 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 71 and 96-115 drawn to a process for treating a transplant recipient to reduce in said recipient an immune response of effector cells against a xenoantigen, comprising administering to a transplant recipient mesenchymal stem cells, wherein T cells are from the donor or from the recipient and the xenoantigen is from the recipient or from the donor, are under consideration in the instant application.

2. Applicant's submission of Terminal Disclaimer has obviated the previous rejection of claims 71 and 96-115 under the judicially created doctrine of obviousness-type double patenting over claims 1-22 of U.S. Patent No. 6,328,960.

In view of the amendment, filed 08/02/04 the following rejection remains:

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

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made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 71 and 96-115 stand rejected under 35 U.S.C. 103(a) as being obvious over WO 01/26470 A1 in view of WO 9623058 for the same reasons set forth in the previous Office Action, mailed on 02/11/04.

Applicant's arguments, filed 08/02/04 have been fully considered, but have not been found convincing.

Applicant asserts that (i) WO'470 is effective only as of its publication date, which is 19 April 2001, whereas the present application has a priority date of 26 October 1999; (ii) WO' 470 teaches only the *in vitro* use of MSCs ; (iii) WO'058 discloses the administration of MSCs along with bone marrow cells and there is no suggestion that MSCs enhance engraftment by suppressing any immune response.

Contrary to Applicant's assertion it is noted that WO' 470 effective priority date under 102(e) is 12 October 1999, because WO'470 was filed after November 29, 2000, designated the US and was published in English. Thus the effective date of WO'470 is prior to the priority date of the instant application. The Supreme Court has authorized 35 U.S.C 103 rejection based on 25 U.S.C 102 (e), see MPEP, 2136.

Applicants have traversed the primary and the secondary references pointing to the differences between the claims and the disclosure in each reference. Applicant is respectfully reminded that the rejection is under 35 USC103 and that unobviousness cannot be established by attacking the references individually when the rejection is based on the combination of the references. see *In re Keller*, 642 F.2d 4B, 208 USPQ 871, 882 (CCPA 1981) See MPEP 2145. This applicant has not done, but rather argues the references individually and not their combination. One cannot show non-obviousness by attacking references individually where the rejections are based on a combination of references. *In re Young* 403 F.2d 759, 150 USPQ 725 (CCPA 1968).

WO'470 teaches a method for treating a transplant recipient to reducing an immune response of the effector cells against alloantigen to the effector cells, comprising administering the suppressor cells (see entire document, Abstract , page 7 lines 10-15 and claims 1-27 in particular). WO'470 teaches that effector cells are T cells (see claim 3 in particular). WO'470 teaches that it has been discovered that mesenchymal stem cell (MSC) can induced antigen-activated T cells to become suppressive for said antigen response and that human suppressor cells can be used in transplantation to ameliorate a response by the immune system to said antigen (see page 2, line 15-22 in particular). WO'470 teaches the suppressor cells are obtained from the donor or from the recipient and co-cultured with MSC *ex vivo* to actually become suppressive. (see page 12 in particular). Though WO'470 does not explicitly teach *in vivo* administration of MSCs , it is noted that WO'470 does not limited only *in vivo* administration

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of suppressor T cells. Moreover, there is no indication that MSC should be removed prior to administering suppressor cells. WO'470 teaches that a transplant is skin, or solid organ (claim 4 and 14,15 in particular). WO'470 teaches that MSC are human MSC (see page 11 in particular). WO'470 teaches that suppressor cells are administered intravenously, prior to/concurrently with and subsequently with transplantation (see page 10, line 10-25 in particular).

WO'470 does not teach a method for treating a transplant recipient to reducing an immune response of the effector cells against xenoantigen to the effector cells, comprising administering mesenchymal stem cells.

WO'058 teaches a method for enhancing bone marrow engraftment in the individual in need thereof comprising administering to said individual a mesenchymal stem cells (see entire document, Abstract and Claims 1-8 in particular). WO'058 teaches that MSC are administered intravenously, prior to/concurrently with and subsequently with transplantation (see page 2 and 3 in particular). WO'058 teaches that administration of MSC is useful to enhance the effectiveness of transplantation (see page 3 in particular)

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of WO'058 to those of WO'470 to obtain a claimed method for treating a transplant recipient to reducing an immune response of the effector cells against xenoantigen to the effector cells, comprising administering mesenchymal stem cells.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because administration of MSC is useful to enhance the effectiveness of transplantation as taught by WO'058 and can be used in method taught by WO'470 to substitute ex-vivo step of co-culturing T cells with MSC cells by direct in vivo administering of MSC into a transplant recipient. It is also noted that alloantigen taught by WO'470 and xenoantigen of the present application are similar in that both antigens can induce an immune response in the transplant recipient and both differ from antigens expressed by the recipient. It is obvious that WO'470 and present application administer the same treatment to achieve the same results. Therefore it would be obvious to one of ordinary skill in the art at the time the invention was made to substitute one type of an antigen i.e. an alloantigen, to the other type of antigen, i.e. xenoantigen in a process for treating a transplant recipient taught by WO'470. When the prior art method is the same as a method described in the specification, it can be assumed the method will obviously perform the claimed process absent a showing of unobvious property. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Semaker. 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). See MPEP 2144. From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

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With regards to Applicant's comments that WO'058 does not suggest that MSCs enhance engraftment by suppressing any immune response.

It is noted that the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Even though applicant has proposed or claimed the mechanism by which MSC enhance engraftment it does not appear to distinguish from the prior art teaching the same or nearly the same method, i.e. administering MSCs to achieve the same endresult. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

5. No claim is allowed.

6. **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

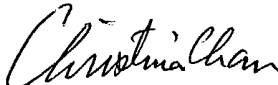
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7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskiy whose telephone number is 571/ 272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/ 272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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August 30, 2004


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